MAK HILL Publications Research Journal of Medical Sciences

Case Series
doi: 10.59218/makrjms.2024.5.574.578

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Key Words
Topical 5-fluorouracil, ocular surface squamous neoplasia, topical chemotherapy, conjunctival hyperemia, photosensitivit

Corresponding Author
K. Gayathri,
Department of Ophthalmology, Kamineni Institute of Medical Sciences, Narketpally, Nalgonda, Telangana, India

Author Designation
[1]Post Graduate
[2]Assistant Professor
[3]Associate Professor
[4]Professor and HOD

Received: 31 January 2024
Accepted: 28 March 2024
Published: 31 March 2024

Citation: Kompalli Rohit Kumar, K. Gayathri, K. Tejaswi and P. Sudhir Babu 2023. Topical 5-Fluorouracil as Primary Treatment for Ocular Surface Squamous Neoplasia: A Case Series Evaluation Res. J. Med. Sci., 18: 574-578, doi: 10.59218/ makrjms.2024.5.574.578

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Topical 5-Fluorouracil as Primary Treatment for Ocular Surface Squamous Neoplasia: A Case Series Evaluation

[1]Kompalli Rohit Kumar, [2]K. Gayathri, [3]K. Tejaswi and [4]P. Sudhir Babu

[1-4]Department of Ophthalmology, Kamineni Institute of Medical Sciences, Narketpally, Nalgonda, Telangana, India

ABSTRACT

Ocular surface squamous neoplasia (OSSN) poses significant challenges in management due to its varied presentation and potential risks associated with surgical interventions. This study explores the safety and efficacy of topical 5-fluorouracil (5-FU) as a sole therapy for OSSN, providing an alternative to surgical approaches. A retrospective analysis was conducted on 10 number of patients diagnosed with OSSN who underwent topical 5-FU therapy as the primary treatment modality. Clinical data including patient demographics, lesion characteristics, treatment regimen and outcomes were collected and analyzed. Topical 5-FU therapy resulted in complete tumor resolution in all patients after a mean of 3 monthly cycles, with no recurrences noted during the follow-up period. Adverse effects were minimal and patient compliance was high. The therapy was well-tolerated, with no significant complications reported. Topical 5-FU emerges as a safe and effective treatment option for OSSN, offering comparable outcomes to surgical interventions while minimizing the risks associated with repeated surgeries. This non-invasive approach provides patients with an alternative to surgery, particularly for those who prefer medical management or are not surgical candidates. Further studies with larger sample sizes and longer follow-up periods are warranted to validate these findings and establish topical 5-FU as a standard therapy for OSSN.

INTRODUCTION

Ocular surface squamous neoplasia (OSSN) presents a spectrum of lesions ranging from mild dysplasia to invasive squamous cell carcinoma (SCC), typically affecting the conjunctiva and cornea[1]. Historically, surgical excision has been the preferred treatment approach for OSSN due to its ability to achieve complete tumor removal. However, this method comes with inherent drawbacks such as high recurrence rates, potential for significant morbidity and the requirement for specialized surgical expertise [2]. In recent years, there has been a notable paradigm shift in the management of OSSN towards the utilization of topical chemotherapy as either a primary treatment modality or as an adjunct to surgery. This shift is motivated by the desire to minimize surgical morbidity while ensuring therapeutic effectiveness. Topical chemotherapy, particularly 5-fluorouracil (5-FU), has gained traction in this context due to its ability to selectively target rapidly proliferating neoplastic cells while sparing normal ocular tissues[3]. The rationale behind utilizing topical chemotherapy lies in its mechanism of action, which involves inhibiting DNA synthesis in actively dividing cells, including cancerous ones. By preferentially targeting these rapidly dividing cells, 5-FU effectively disrupts the growth and proliferation of the tumor, leading to regression and, ideally, complete resolution of the neoplastic lesion[4].

Despite the increasing adoption of topical 5-FU in OSSN management, there remains a critical need for comprehensive evaluations of its efficacy and safety as a primary treatment modality[5]. This is particularly crucial given the potential implications for patient outcomes and treatment protocols. Therefore, the primary objective of this study is to rigorously assess the effectiveness of topical 5-fluorouracil 1% (5-FU) as the primary treatment for OSSN through a retrospective case series analysis. By conducting a detailed retrospective review of cases where OSSN was treated solely with topical 5-FU, we aim to gather robust data on treatment outcomes, including tumor regression, recurrence rates and adverse effects. This thorough analysis will provide valuable insights into the role of topical 5-FU in OSSN management and its potential as an alternative to traditional surgical excision. Furthermore, by elucidating the efficacy and safety profile of topical 5-FU in this context, we aim to inform clinical decision-making and optimize treatment strategies for OSSN. Ultimately, our goal is to contribute to the advancement of evidence-based practices in ocular oncology, with the overarching aim of improving patient outcomes and quality of care for individuals affected by OSSN.

MATERIAL AND METHODS

This clinical case series study was conducted at Kamineni Medical Hospital in Narketpally, Telangana, over a period of 8 months. A total of 10 patients diagnosed with ocular surface squamous neoplasia (OSSN) were included in the study. Patients ranged in age from 30-80 years. The study protocol was approved by the institutional review board. Informed consent was obtained from all participants prior to enrollment in the study. Patient confidentiality was maintained throughout the study period.

Inclusion Criteria:

- Patients diagnosed with OSSN
- Tumor size less than 4mm

Exclusion Criteria:

- Patients with tumor size greater than 4mm
- Patients with recurrent lesions

Procedure:

Clinical Diagnosis: Patients were clinically diagnosed with OSSN through slit lamp examination.

Imaging: Anterior segment optical coherence tomography (AS-OCT) was performed to assess lesion characteristics and extent.

Treatment Regimen: Patients were treated according to the protocol established by Mudduveerappa *et al*. (source: IP International Journal of Ocular Oncology and Oculoplasty, 2023;9(1):46-49). Topical chemotherapy with 5-fluorouracil (5-FU) 1% was utilized. The treatment regimen consisted of applying 5-FU topically four times per day for one week, followed by a drug holiday of three weeks, constituting one treatment cycle.

Monitoring: Patients were monitored for treatment response clinically and through AS-OCT imaging. Treatment was continued until complete resolution of the lesions was confirmed.

Assessment of Side Effects: The incidence of various side effects associated with topical 5-FU therapy was monitored throughout the treatment period.

Follow-Up: Patients were followed up for a period of three months post-treatment to evaluate long-term outcomes and recurrence rates.

Data Collection: Patient demographics including age, gender and previous history of OSSN were recorded.

Lesion characteristics such as size and location were documented. Treatment response, including resolution of lesions and recurrence rates, was assessed. Adverse effects of topical 5-FU therapy were documented.

Statistical Analysis: Statistical tests used for comparing the efficacy of antibiotics were described, with a significance level set at $p<0.05$. The median age of the patients in the sample is calculated to be 54.8 years. The majority of patients fall within the 50-60 age range, constituting 50% of the sample, while the remaining patients are distributed across the other age brackets. (Table 2) shows, the majority of individuals are male (80%) compared to females (20%). All cases of laterality are unilateral (100%), with no instances of bilateral cases. Concerning vision, 23% of the sample population exhibits a vision status of less than 6/60, while the majority (77%) has a vision status exceeding 6/60.

The (Fig 1) illustrates that among the identified risk factors, old age is the most prevalent, accounting for 37% of the sample population. Excessive sun exposure follows closely behind at 32%, while smoking and prior skin lesions are each reported in 21% and 5% of the population, respectively. Immuno-compromised status is the least prevalent risk factor, found in only 5% of the individuals studied. The (Table 3) reveals that within the sample population, the most prevalent symptom is the sensation of a foreign body, reported by 43% of individuals. Chronic redness follows at 21%, while watering eyes and being asymptomatic are observed in 29 and 7% of the population, respectively. The (Table 4) depicts the prevalence of various side effects resulting from 5-FU treatment. Conjunctival hyperemia is the most frequently reported side effect, affecting 30% of individuals. Irritation and watering eyes follow closely behind at 25 and 20%, respectively. Photosensitivity is also observed in 20% of patients. Additionally, superficial punctate keratopathy is noted in 5% of the treated population.

The presentation displays the progression of treatment for a corneal condition. Pre-cycle images reveal a cloudy cornea with irregularities, while post-cycle images show a clear cornea with a smooth surface, indicating successful treatment with topical therapy, as evidenced by both clinical photos and OCT scans In this Case patient has redness, foreign body sensation, growth near nasal limbal area as seen in clinical photos and OCT scans. After treatment cycles, redness and growth decreased as shown in pos cycle image and oct. In this Case patient underwent topical therapy for an eye condition. Before treatment, the eye exhibited redness, swelling and an open sore, as seen in clinical photos and OCT scans. After several treatment cycles, redness and swelling decreased significantly and the sore appeared healed, demonstrating the effectiveness of topical therapy in improving the eye condition.

RESULTS AND DISCUSSIONS

The study presented here highlights the efficacy of topical chemotherapy, specifically 5-fluorouracil (5-FU), as a sole therapy for ocular surface squamous neoplasia (OSSN). OSSN lesions range from dysplasia to invasive squamous cell carcinoma, often involving critical ocular structures like the cornea, conjunctiva and limbus. The clinical appearance of these

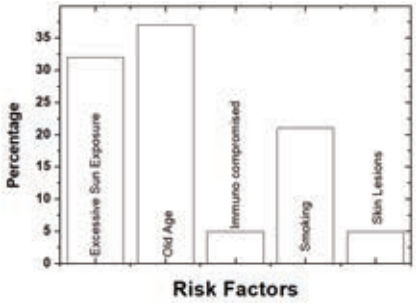

Fig. 1: Frequency of Risk Factors in a Sample Population

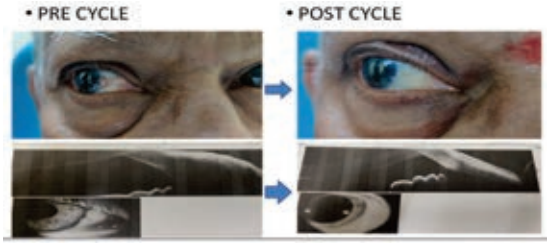

Fig. 2: The presentation displays the progression of treatment for a corneal condition. Pre-cycle images reveal a cloudy cornea with irregularities, while post-cycle images show a clear cornea with a smooth surface, indicating successful treatment with topical therapy, as evidenced by both clinical photos and OCT scans

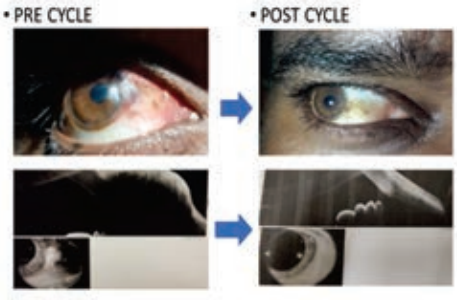

Fig. 3: In this Case patient has redness, foreign body sensation, growth near nasal limbal area as seen in clinical photos and OCT scans. After treatment cycles, redness and growth decreased as shown in pos cycle image and oct

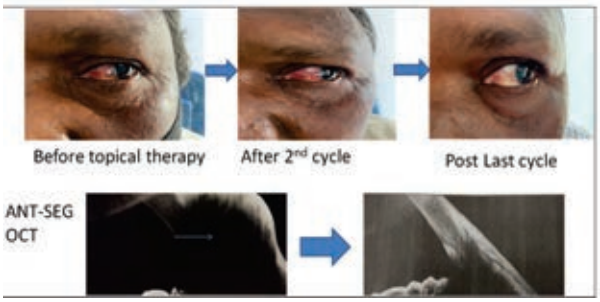

Fig. 4: In this Case patient underwent topical therapy for an eye condition. Before treatment, the eye exhibited redness, swelling and an open sore, as seen in clinical photos and OCT scans. After several treatment cycles, redness and swelling decreased significantly and the sore appeared healed, demonstrating the effectiveness of topical therapy in improving the eye condition

Table 1: Distribution of Patient Ages in a Sample of 10 Patients

Age Range	No. of Patients
30-40	1 (10%)
40-50	3 (30%)
50-60	5 (50%)
60-80	1 (10%)
Total	10

Table 2: Distribution of Gender, Laterality and Vision in a Sample

Category	Frequency (%)
Gender	
Males	8 (80)
Females	2 (20)
Laterality	
Unilateral	10 (100)
Bilateral	0 (0)
Vision	
<6/60	3 (23)
>6/60	7 (77)

Table 3: Frequency of Symptoms in a Sample Population

Symptom	Frequency (%)
Asymptomatic	1 (7)
Chronic Redness	3 (21)
Foreign Body Sensation	6 (43)
Watering	4 (29)

Table 4: Frequency of Side Effects of 5-FU Treatment

Side Effect	Frequency (%)
Conjunctival Hyperemia	6 (30)
Irritation	5 (25)
Photosensitivity	4 (20)
Watering	4 (20)
Superficial Punctate Keratopathy	1 (5)

lesions is characteristic and high-resolution optical coherence tomography (HR-OCT) reveals hyper-reflective, thickened epithelium with an abrupt transition between normal and cancerous tissue[6].

The recent advancements in the management of Ocular Surface Squamous Neoplasia (OSSN) have marked a significant shift from surgical excision to topical chemotherapy, with 5-fluorouracil (5-FU) gaining prominence due to its targeted action on proliferating neoplastic cells[7]. In the current study of 10 patients, the application of topical 5-FU across 3 median cycles resulted in no cases of recurrence, which is particularly notable. The only side effect observed was conjunctival hyperemia. The absence of recurrence suggests a potential efficacy of topical 5-FU in treating OSSN, presenting a promising alternative to surgical methods. The side effect profile appears to be limited and manageable, which is encouraging for the prospect of topical chemotherapy in ocular oncology. When compared with earlier studies, Parrozzani *et al*.'s study with a relatively larger cohort of 45 patients shows a recurrence rate of 7.3% with just a single cycle of treatment, which is considerably higher compared to the current study[8]. Another study by Nandini Venkateswaran *et al*. demonstrates a 3.3% recurrence rate with a median of 2.4 cycles, offering a middle ground in terms of efficacy. An additional side effect noted in this cohort is photosensitivity, which has not been reported in the current study[9].

A study conducted by Thomas *et al*. with 13 patients resulted in a 2.5% recurrence rate after 2 cycles of treatment, indicating that even with fewer patients, the treatment was effective to a considerable degree. Like the current study, the side effect reported was conjunctival hyperemia, reinforcing the tolerability of the treatment[10]. Whereas, the study by Mudduveerappa *et al*. mirrors the outcomes of the current study in terms of recurrence, which stood at 0% with 3 median cycles of treatment. However, their study reports an additional side effect of photosensitivity along with conjunctival hyperemia. The consistency in the recurrence rate with the current study, despite the additional side effect, adds to the evidence supporting the use of topical 5-FU[11].

CONCLUSION

The findings of this study show the potential of topical 5-FU chemotherapy as a safe, effective and patient-friendly treatment option for OSSN. The comparison suggests that the current study's findings are in line with previous research, Future studies with larger sample sizes and longer follow-up periods are warranted to further validate these findings and establish topical chemotherapy as a standard therapeutic approach for OSSN.

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